IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

TITBALL et al Atty. Ref.: **3974-3**

Continuation of Serial No. **08/894,527** Group:

Filed: **November 20, 2001** Examiner:

For: **PHARMACEUTICALS AND ASSAYS USING ENZYME SUBUNITS**

* * * * * * * * * * * *

November 21, 2001

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Preliminarily amend the above-identified application as follows.

IN THE SPECIFICATION

Amend the specification as follows.

Page 1, before line 1, insert the following:

--This application is a continuation of application Serial No. 08/894,527 filed March 16, 1998, which in turn is a 35 U.S.C. 371 of PCT/GB96/00380 filed February 21, 1996, and claims benefit to GB 95 03486.4, filed February 22, 1995.--

IN THE ABSTRACT

Insert the attached ABSTRACT after the claims.

IN THE DRAWINGS

Authorization to amend sheet 1 of the drawings as shown in the attached Letter to the Chief Draftsperson is requested.

IN THE CLAIMS

Cancel claims 1-31, without prejudice.

Add the following claims:

--32. (new) A pharmaceutical composition comprising an antibody conjugated to a lipase able to lyse liposomes or a lipase component having no or less lipase activity in comparison to a corresponding lipase holoenzyme and, optionally a pharmaceutically acceptable carrier, diluent or excipient, said lipase component being selected from the group consisting of N-terminal recombinant CPAT and C-terminal recombinant CPAT.

33. (new) A pharmaceutical composition comprising a pharmaceutical agent protected in a liposome wherein the liposome is associated with or integrally contains a second lipase component able to reconstitute lipase activity when contacted with first lipase component bound to an antibody.

34. (new) A pharmaceutical package comprising in a first container a pharmaceutical composition comprising a composition comprising an antibody conjugated to a lipase able to lyse liposomes or a lipase component having no or less lipase activity in comparison to a corresponding lipase holoenzyme and, optionally a pharmaceutically acceptable carrier, diluent or excipient and, in a second container, a

composition comprising a pharmaceutical agent protected in a liposome which can be lysed by a lipase and, optionally, a pharmaceutically acceptable carrier, diluent or excipient.

35. (new) A pharmaceutical package comprising in a first container a pharmaceutical composition comprising a composition comprising an antibody conjugated to a lipase able to lyse liposomes or a lipase component having no or less lipase activity in comparison to a corresponding lipase holoenzyme and, optionally a pharmaceutically acceptable carrier, diluent or excipient and, in a second container, a composition of claim 33.

36. (new) A composition of claim 33 wherein at least one of said first lipase component or said second lipase component is N-terminal recombinant CPAT or C-terminal CPAT.

37. (new) A package of claim 34 wherein said lipase component is N-terminal recombinant CPAT or C-terminal CPAT.

38. (new) A package of claim 35 wherein said lipase component is N-terminal recombinant CPAT or C-terminal CPAT.--

REMARKS

Claims 1-31 have been canceled, without prejudice.

Claims 32-38 have been added.

An early and favorable Action on the merits is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
B. J. Sadoff
Reg. No. **36,663**

BJS:eaw
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

ABSTRACT OF THE DISCLOSURE

A method of releasing an agent for example, a chemotherapeutic, under predetermined conditions by protecting the agent within a lipid structure such as a liposome, causing lipase activity to be constituted by combining two or more components, e.g., recombinant N- or C-terminal *Clostridium perfringens* alpha-toxin fragments, one of these components being conjugated to a targeting molecule e.g., an antibody which binds to a target such as a tumor antigen. The lipid structure is then exposed to the constituted lipase activity such as to release the agent. Also disclosed are materials and kits for use in the method.

MARKED UP SPECIFICATION AND CLAIMS

Page 1, before line 1, insert the following:

--This application is a continuation of application Serial No. 08/894,527 filed March 16, 1998, which in turn is a 35 U.S.C. 371 of PCT/GB96/00380 filed February 21, 1996, and claims benefit to GB 95 03486.4, filed February 22, 1995.--